UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/499,006	02/04/2000	Dr. Paddy Jim Baggot	249/127	9604

34313 7590 06/09/2006

ORRICK, HERRINGTON & SUTCLIFFE, LLP
IP PROSECUTION DEPARTMENT
4 PARK PLAZA
SUITE 1600
IRVINE, CA 92614-2558

EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/499,006	BAGGOT, DR. PADDY JIM	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 15-24* is/are pending in the application.

4a) Of the above claim(s) *1 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-16 and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL REJECTION

1. This action is responsive to the Amendment and Response filed 30 March 2006. Claims 22-23 have been amended, and claims 15-16 and 18-24 are under consideration. Claims 1 and 17 remain withdrawn from consideration (see paragraph 3, below). Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

3. Claims 1 and 17 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

Claim Rejections - 35 USC § 112, first paragraph

4. Claims 15-16 and 18-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying Down Syndrome in a fetus in which decreased levels of formiminoglutamic acid in amniotic fluid (as compared to a normal control) and/or increased levels of oxalic acid in amniotic fluid (as compared to a normal control) are detected, does not reasonably provide enablement for methods in which abnormal levels of any metabolite or combination of metabolites identified in amniotic fluid is considered to be indicative of Down Syndrome. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the reasons set forth in the prior Office action of 30 September 2005.

The response traverses the rejection for the reasons set forth below. Applicant's arguments have been thoroughly considered but are not persuasive for the reasons that follow.

First, it is noted that the examiner agrees that it is well within the ability of one skilled in the art to measure metabolites by a variety of methods, including via the use of a GC/MS device, and to produce and compare control and patient profiles, etc. Further, it is agreed that one skilled in the art could clear perform a "multiplex analysis" of a sample and examine "a plurality of variations in" a profile.

With regard to Applicant's argument that the "question of whether the method can be practiced does not depend on analyzing any particular metabolite with a mathematical formula that is predetermined for any particular metabolite," the examiner also agrees that enablement of the claims does not require analysis "with a mathematic formula that is predetermined for any particular metabolite." However, it is noted that the rejection made by the examiner in the Office action of 30 September 2005 did not assert that such an analysis was required.

The response then argues that "the Examiner does not appear to believe that the differences that are revealed by the measurements provided by the claimed method are adequate for the clinician to identify the presence of Down Syndrome in a fetus by performing the appropriate comparison," and that "this is not a suitable ground for rejection...because any doubt as to whether or not the invention functions as the

application claims does not equate to whether one of ordinary skill in the art could actually perform the method as claimed without undue experimentation." The response further states that "the Examiner is not questioning whether or not excess experimentation is required, the Examiner is disputing whether or not the method recited actually enables the clinician to successfully accomplishes [sic] the goal of the method as claimed," and urges that the claims recite and specify how the method is performed and that "The fact that the comparison requires a multi-factor analysis cannot require undue experimentation" under 35 USC 112. The response continues that "the skilled judgment of one of ordinary skill in the art as described in the specification" would allow such an artisan to "identify the presence of a disease condition based on a number of individual measurements of underlying biochemical mechanism," and Applicant offers to establish through declaratory evidence that the method may be practiced by an ordinary artisan. Finally, the response refers to *PPG Industries v. Guardian Industry Corporation,* 75 F.3d 1558, 1564 (Fed. Cir. 1996), stating that the "Federal Circuit has also noted that a considerable amount of experimentation is permissible when it is routine or provided by reasonable guidance in the application."

These arguments have been thoroughly considered but are not persuasive. First, it is again noted that the examiner does not dispute the ability of a skilled artisan to analyze samples for metabolites, to perform a multiplex analysis, to generate metabolite profiles, etc. Further, as stated in the prior Office action, the examiner does believe that the claims are enabled in part. However, the instant claims are not drawn, e.g., to a method of analyzing or profiling a sample of amniotic fluid, such that the

claims would merely require one to perform steps of, e.g., obtaining a sample, analyzing the sample, compiling a profile, etc., in order to enable the claims. Rather, the claims are drawn to methods of identifying Down Syndrome; thus, the method that one must be able to practice without undue experimentation is one that results in "identifying Down Syndrome." It is suggested that Applicant re-read the final step of independent claims 15 and 21: claim 15 recites a step of "identifying the presence of Down Syndrome in the fetus when the comparing step of step d) reveals that the profile of metabolites in the amniotic fluid specimen compiled in step c) differs from the control profile," while claim 21 states "identifying the presence of Down Syndrome in the fetus based on the identified plurality of abnormal quantities of metabolites compared to the quantity of each metabolite in the control profile." While Applicant appears to be arguing that the claims are in some way limited to methods in which only particular types of profiles (e.g., profiles determined by a physician or other practitioner, based on guidance provided in the specification, to be indicative of Down Syndrome) would result in "identifying the presence of Down Syndrome," the claims as written encompass methods in which any difference in metabolic profile (claim 15) or any "plurality of abnormal quantities of metabolites" (claim 21) results in "identifying the presence of Down Syndrome." Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, as discussed in *MPEP* 2164.08 with regard to considering whether claims are enabled in a manner commensurate with the scope with claims, "The examiner should determine what each claim recites and

what the subject matter is when the claim is considered as a whole, not when its parts are analyzed individually." Thus, it is not sufficient for the various individual steps of a method to be enabled; rather, the claimed invention as a whole must be enabled. The instant claims lack enablement because, while the specification teaches only a few particular abnormal profiles that are indicative of Down Syndrome, the claims as written encompass methods in which any type of abnormality in a profile would be considered indicative of Down Syndrome. While one of skill in the art could clearly perform further experiments aimed at identifying additional types of abnormal profiles that might be indicative of Down Syndrome, the outcome of such experiments cannot be predicted; thus, it is unknown whether any quantity of experimentation would be sufficient to allow one to practice the invention as claimed more broadly. Further, as was noted in the prior Office action, the vast majority of metabolites present in amniotic fluid do not appear to differ significantly in Down Syndrome patients as compared to normal patients. Thus, for example, were one of skill in the art to identify in a sample abnormal levels of a "plurality of metabolites" which are shown in Applicant's specification to typically be present at normal levels in Down Syndrome patients, it would be completely unpredictable as to whether such abnormal levels could be relied upon as indicating the presence of Down Syndrome (and in fact, Applicant's own data would not support such a conclusion). Further, even a vast, unlimited quantity of experimentation would not be sufficient to enable "identifying Down Syndrome" based on an abnormal profile of metabolites that is simply unrelated to Down Syndrome; such a quantity and type of experimentation is neither routine nor "provided by reasonable guidance in the

application," and is certainly undue. Thus, Applicant's arguments are not persuasive with regard to the instant claims, and this rejection is maintained.

Claim Rejections - 35 USC § 112, second paragraph

5. With regard to the prior rejection of claims 22-23 over the recitation of the limitation "the identifying step," it is noted that Applicant's amendment clarifies which identifying step is further limited by the claims. Accordingly, the rejection is withdrawn.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS:

6. Claims 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is noted that the amendment discussed immediately above (see paragraph 5) makes clear that the determination of whether metabolite levels are "increased" or "decreased" is made with respect to "the quantity for that respective metabolite of the control profile" (see language of claim 21). However, the amendment of the claims to add the language "and concentrations thereof" renders claims 22-23 vague and indefinite because it is unclear what is further required by this language. It is noted that claims 22-23 already require the identification of "quantities of metabolites," and the identification of increased or decreased concentrations thereof relative to a control level. Thus, it is not clear what further measurement or calculation (if any) is necessitated by the additional claim language "and concentrations thereof." Clarification is required.

It is further noted that while Applicant has amended the claims to refer to "concentration of" each metabolite in claim 23 (including formiminoglutamic acid) and to all but one of the metabolites of claim 22, claim 22 has not been amended with respect to formiminoglutamic acid. While this discrepancy does not render claim 22 indefinite, it is called to Applicant's attention as a courtesy, as it appears that this may have been inadvertent.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is

571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634

6/6/2006